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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/633,295	08/07/2000	Alfons Nichtl	100564-00025	4590

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EXAMINER
DO, PENSEE T

ART UNIT	PAPER NUMBER
1641	19

DATE MAILED: 05/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/633,295	NICHTL, ALFONS	
	Examiner	Art Unit	
	Pensee T. Do	1641	

--The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

THE REPLY FILED 12 March 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☒ Applicant's reply has overcome the following rejection(s): *112, 2nd*.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *24-39*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

ADVISORY ACTION

Amendment Entry & Claim Status

The after-final amendment filed on March 12, 2003 has been acknowledged and entered.

Claims 24-39 are pending.

Withdrawn Rejection(s)

Rejection under 35 USC 112, 2nd paragraph in the previous office action is withdrawn herein.

Maintained Rejection(s)

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this

application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 24, 30, 31 and 33 are rejected under 35 U.S.C. 102(e) as being anticipated by Liberti et al. (US 5,597,531).

Liberti teaches a coating process comprising coating a wide range of materials (including dextran, proteins, synthetic polypeptides, polymers, detergents, polyethylene glycol and combinations thereof) onto colloidal magnetically responsive particles to obtain stable microagglomerants. The process comprises the following steps:

(a) forming a liquid mixture of a particulate magnetic starting material and a coating material;

(b) treating the mixture to subdivide the particles of the magnetic starting material;

(c) permitting the coating material to form a coating on the subdivided particles of the magnetic starting material to form stable, resuspendable coated particles;

(d) recovering the resuspended coated magnetic particles from the liquid mixture. (See col. 4, lines 45-52; claim 1).

Claim Rejections - 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 25-29, 32 , 34-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liberti et al. (US 5,597,531) further in view of Nichtl et al. (US 5,972,720).

Liberti teaches a coating process comprising coating a wide range of materials (including dextran, proteins, synthetic polypeptides, polymers, detergents, polyethylene glycol and combinations thereof) onto colloidal magnetically responsive particles to obtain stable microagglomerants. The process comprises the following steps:

(a) forming a liquid mixture of a particulate magnetic starting material and a coating material;

(b) treating the mixture to subdivide the particles of the magnetic starting material;

(c) permitting the coating material to form a coating on the subdivided particles of the magnetic starting material to form stable, resuspendable coated particles;

(d) recovering the resuspended coated magnetic particles from the liquid mixture. (See col. 4, lines 45-52; claim 1).

Liberti also fails to teach an additional stabilizer such as an inert protein or/and polyethylene glycol after loading the colloidal particles and colloidal particles selected from the group consisting of gold, silver, copper, platinum, palladium and mixture thereof.

Nichtl teaches that after the colloidal particles have been loaded with the respective desired biomolecule, it is necessary to stabilizer the conjugates. This stabilization minimizes an aggregation of the particles and to saturate the remaining free surfaces accessible to adsorption. In the state of the art inert proteins, e.g. bovine serum albumin, detergents, and polymers such as polyethylene glycol, polyvinylpyrrolidone, polyvinyl alcohol, polyvinyl sulfate, dextran and gelatin are used as stabilizers. Nichtl also teaches a new stabilizer, thiol-substituted polyethylene glycol, which is added to the conjugate of gold particles or metallic particles such as particles of metals, metal oxides, metal hydroxides, metal compounds or particles coated with metals or metal compounds. The metal particles are selected from the group consisting of gold, silver, copper, platinum, palladium, and mixture thereof. (see col. 1, lines 47-61; col. 2, lines 25-28; col. 2, line 53-col. 3, line 7).

It would have been obvious to one of ordinary skills in the art to add the an inert protein selected among those taught in Nichtl to the conjugate formed by the method of Liberti since Liberti and Nichtl both teach improving the long-term stability of the conjugates and lowering the aggregation or agglomeration tendency in solution. (see Nichtl col. 2, lines 25-36).

Response to Arguments

Applicant's arguments filed March 12, 2003 have been fully considered but they are not persuasive.

Regarding the 102 rejection, Applicant submits that since Liberti et al. emphasize that it is important to select a coating material that produces a coating that remains intact when the coating particles are removed from suspension in order to produce resuspendable coated particles product in distinguishing their invention from the prior art, the Liberti methods are designed to produce a coating that allows coated but agglomerated materials to be resuspendable by chemical or by mechanical means, such as sonication. "Stability" of these particles refers to the stability of the suspendability of the particles and not to the function of the particles. Applicant also submits that the particles of the present invention do not aggregate to the extent of the prior art particles and have a coating of biomolecules that is not displaced from the surface by detergent.

Applicant's argument is not on point because the claims fail to require that the stability must refer to the function of the particles. Furthermore, the detergent coating is not the only coating on the particles in Liberti et al. Liberti teaches that a wide range of materials such as protein, polymers, detergents and *combination thereof* can be coated on the particles. (see col. 4, lines 48-52). Thus, the coating mixture can contain detergent. Since the claims contain opening language, they can include other functions or limitations such as aggregation. Also, Liberti et al. does not teach that the biomolecules are displaced from the surface of the particles by detergent. The role of the detergent is to stabilize the particles, not to displace the biomolecules. Liberti's method teaches a coating of detergents, protein or a combination thereof is coated on the particles and thus meets the requirements of the present invention because with the

same components and the same method steps, the results should be the same. Since stabilizing is not an adverse effect, the particle of Liberti meets the limitation of 'the detergent does not adversely influence the function of the conjugates by displacing the biomolecules or by interacting with the biomolecules or the colloidal particles. Thus, Liberti's particles meet the requirements of the present invention.

Regarding the 103(a) rejection, Applicant argues that Nichtl is cited for teaching use of a stabilizer to minimize aggregation of particles and to saturate free surfaces on the particles. This teaching is not make up for the lack of disclosure in Liberti concerning the use of detergent which does not adversely influence conjugate function by displacing the biomolecules from the particle surface or by interacting with the biomolecule or the particle. Nichtl teaches that stabilizers of the prior art, including detergents, bind adsorptively to free surfaces of metal particles and proposes using polyethylene glycol stabilizer to avoid the problems of the prior art. Nitchtl therefore teaches away from using detergents in biomolecule-particle conjugates as the present claims require.

Since Liberti has been discussed above. No further discussion is needed regarding the use of detergent which does not adversely influence conjugate function by displacing the biomolecules from the particles surface or by interacting with the biomolecule or particle. Nichtl is relied for the additional stabilizer, not the use of detergents. Nichtl teaches adding an additional stabilizer after the particles have been coated (regardless of the coating material). Thus, Applicant's claim of Nichtl teaching

away from using detergents as a stabilizer after coating, which is a non-required limitation by the present invention, is irrelevant. Thus, the rejections are still maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 703-308-4398. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-746-5291 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Pensee T. Do
Patent examiner
April 30, 2003

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP 1800/1641
5/2/03